

1 100 200 300 400 500 600 700 800 900 1000 1100 1200 1300 1400 1500 1600 1700

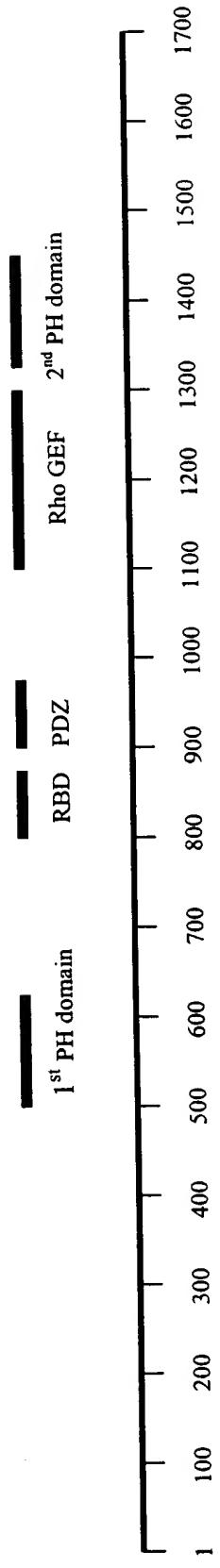


FIG. 1

PH: domain 1 of 2, from 507 to 620: score 65.9, E = 4.1e-17  
\*->vikeGwLlkks.....kswkRyfvLfnnvLlyykds  
v + GwL+ k + +++++ + + +wk+++++L++ +Ll+y+  
33521 507 VRRAGWLFFKPltvqkerklelvarRKWKQYWVTLKGCTL LFYETY 553

k.....kkpkgsipLsgcqvek.pd....kncFeirt.dr.tlllqae  
++++ +++++ p+ + +++++v p++++++n+F+++++ ++++++l+qa+  
33521 554 GknsmdqssAPRCALFAEDSIVQSvPEhpkkENVFCLSNsFGdVYLFQAT 603

seeerkeWvkaiqsair<-\* (SEQ ID NO:4)  
s+ +++ Wv+a +sa++  
33521 604 SQTDLENWVTAVHSACA 620

**FIG. 2A**

RBD: domain 1 of 1, from 810 to 873: score -3.0, E = 2.3  
\*->ktirvhLPnnqrsVvevRpGmtvrDaLakalkkRGLnpsacvVrrsg  
+ vh +n ++V +p +v+D+L a+k+R+L ps +  
33521 810 IQTYVHFQDNHGVTVGIKPEHRVEDILTLACKMRQLEPSHYGLQ--- 853  
dpqeGekkpLdldtdissLpgPeElvvEnl<-\* (SEQ ID NO:5)  
L+ d + + +p+P +E  
33521 854 -----LRKLVDDNVEYCIPAP----YEYM 873

**FIG. 2B**

PDZ: domain 1 of 1, from 890 to 975: score 33.5, E = 4.8e-06  
\*->eitlekevkrgglGfsikggsdk.....givvsevlpGsgaAeagGr  
+++l k + +Gf + + d++++ + i++s+vlp+ g A G  
33521 890 DVQLTKTGSVCDGFATQVDERqhlsRIFISDVLPD-GLAYGEG- 934

LkeGDvI1svNGqdvenmsheravlaikgsgg.evtLtv1Rd<-\*(SEQ ID NO:6)  
L++G I+ NG+ v+++ ++++++a+ + ++ +tL +++  
33521 935 LRKGNEIMTLNGEAVSDL-DLKQMEALFSEKSvGLTLIARPP 975

**FIG. 2C**

RhoGEF: domain 1 of 1, from 1103 to 1292: score 147.0, E = 3.3e-40  
\*->v1kElleTEkkYvrdLeildnvymkpLreaaisskpvltpddietiF  
v+ E1+ TEk Yv+dL 1 y++pL+++ +lt+d++e++F  
33521 1103 VIQELVDTEKSYVKDLSCLFELYLEPLQNET-----FLTQDEMESLF 1144

sNiediyefhreFLkssLearisssqfedlDe....kkiepsaprlGdlF  
+ +++ +ef++ FL Let is+s d + +++ + 1G F  
33521 1145 GSLPEMLEFQKVFLE-TLEDGISAS--SDFNTletpSQFRKLLFSLGGSF 1191

1klkepflqvYgeYcsnkpyAqellekrlrqaasnpqFaefldeveassnt  
l + ++ +++Y +c+n+ +q++le+ a++ +F+ fld + + +  
33521 1192 LYY-ADHFKLYSGFCANHIKVQKVLER--AKTDKAFKAFLDARNPTKQH 1237

gAkddavkltLqsLLlkPvqRilrYpLLLkeLLkhtpegedqpdredLkk  
tL+s+L+kPvqR+l+YpLLLkeL+++t+ +++++ L +  
33521 1238 S-----STLESYLIKPVQRVLKYPLLKELVSLTDQ--ESEEHYHLTE 1278

aldllqdlaksiNe<-\* (SEQ ID NO:7)  
al++++ +a++iNe  
33521 1279 ALKAMEKVASHINE 1292

**FIG. 2D**

PH: domain 2 of 2, from 1353 to 1455: score 4.3, E = 8.7  
\*->fvLfnnvLyykdsk.....kkpkgsipLsg  
fv+++ v+1 yk+ + +++ ++++++ +++++ +++k + ip+s  
33521 1353 FVFKRAVILVYKENC1kkklpsnsrpahnstdldpFKFRWLIPISA 1399

cqvek.pd.....kncFeirt.dr.....t111qaeseeerkeWvka  
+qv+ + +++++ +e++++ + ++++++ + l+++++e++ vk  
33521 1400 LQVRLgNPagtenNSIWEIHTKSeiegrpetIFQLCCSDSESKTNIVKV 1449

iqsair<-\*(SEQ ID NO:8)  
i+s+r  
33521 1450 IRSILR 1455

**FIG. 2E**

PH\_update: domain 1 of 2, from 507 to 622: score 63.3, E = 5.2e-15  
\*->vikeGwLlkks.....k.swkkryfvLfngvLlyyksk  
v + GwL k + ++ ++ +++wk+++++L++ +Ll+y+  
33521 507 VRRAGWLFFKPltvqkerklelvaRrKWKQYWVTLKGCTLLFYETY 553  
.....kpkgsipLsgcsvre.p.....cFeivt.dr.tlllqAe  
++++ ++++++p+ ++ ++ +v+ p++++++F+++++ ++++=+qA  
33521 554 gknsmdqssAPRCALFAEDSIVQSVPehpkkenVFCLSNsFGdVYLFQAT 603  
seeereewvealqsaika<-\* (SEQ ID NO:9)  
s+ ++e Wv+a +sa+a++  
33521 604 SQTDLENWVTAVHSACASL 622

**FIG. 3A**

RBD\_5: domain 1 of 1, from 810 to 881: score 68.6, E = 1.3e-16  
\*->ktcrvhLPdnqrtvVkvRPGktvrDaLakaLkkRgLnpeacvVrlrg  
+---+vh++dn +---+V ++P+++v+D+L +a+k+R+L+p++++++lr+  
33521 810 IQTYVHFQDNHGVTVGKPEHRVEDILTLACKMRQLEPSHYGLQLRK 856  
dpqeGekkpldlnqdissLagqElvveel<-\* (SEQ ID NO:10)  
++ ++ + ++ +----+q +v++e+  
33521 857 L---VDDNVEYCIPAPYEMQQQVYDEI 881

**FIG. 3B**

pdz\_new: domain 1 of 1, from 900 to 976: score 39.3, E = 8.9e-08  
\*->gglGfsivg.....gifvssvvpGspAakaGrkslglLkvGDv  
+Gf ++ + +++++ + if+s+v+p++ A+ G L++G +  
33521 900 CDFGFAVTaqvderqhlsRIFISDVLPDGLAYGEG-----LRKGNE 940  
IleVNGetsvegltheeavd11kkaggggvGekvtLtv1Rgg<-\* (SEQ ID NO:11)  
I+ NG + v++l+ + +l + + +tL+ +++  
33521 941 IMTLNG-EAVSDLNLKQMEALFSEKSV-----GLTLIARPPD 976

**FIG. 3C**

RhoGEF\_3: domain 1 of 1, from 1103 to 1292: score 217.7, E = 1.8e-61  
 \*->v1kELLqTErnYVrdLkilvevflkpLkkeakssllplspdevktl  
 v++EL++TE++YV+dL +l e +l+pL++e +l++de+++1  
 33521 1103 VIQELVDTEKSYVKDLSCLFELYLEPLQNET-----FLTQDEMESL 1143

FgpNieeiyefHrrFLdeLeerveewllskdl.Ksernsviedsgerigd  
 Fg ++e +ef++ FL++Le+ ++ + d++ e+ s++++ +g  
 33521 1144 FG-SLPEMLEFQKVLETLEDGISASS---DFnTLETPSQFRKLLFSLGG 1189

vFlklsaeeffkiYseYcsnhpdalellkkLmkkknpaFqkflkeies  
 F1 + +++fk+Ys +c+nh + ++l+ +k+++aF++f1+ +  
 33521 1190 SFLYY---ADHFKLYSGFCANHIKVQKVLER---AKTDKAFKAFLDARNP 1233

kpncrsksearltLes1LikPvQR1tkYpLLLkellkhtppdhedredLk  
 +++++ tLes+LikPvQR++kYpLLLkel t+ ++e++ +L+  
 33521 1234 TKQHS-----STLESYLIKPVQRVLKYPLLKELVSLTDQESEEHYHLT 1277

kAleaikelasqvNe<-\* (SEQ ID NO:12)  
 +Al+a++++as++Ne  
 33521 1278 EALKAMEKVASHINE 1292

**FIG. 3D**

PH\_update: domain 2 of 2, from 1326 to 1457: score 17.7, E = 0.28  
\*->vikeGwLlkks.....k.swkkryfvLfngvLlyyksk.....  
+++++ +++++ + + ++ ++ fv+++ v+l yk+ + +++  
33521 1326 LLMHSTVSWLNpf1slgkaRkDLELTVFVFKRAVILVYKENck1kkk 1372  
.....kpkgsipLsgcsvre.p.....cFeivt.d  
++++++ +++++ ++ k + ips ++vr + + + ++++ +e++++  
33521 1373 lpsnsrpahnstdldpfKFRWLIPISALQVRLgNpagtennsIWELIhtK 1422  
r.....t111qAeseeereeeWvealqsaiaaka<-\* (SEQ ID NO:13)  
+ ++++++ + l+++++e+++ vt ++s +++++  
33521 1423 SeiegrpetIFQLCCSDSESKTNIVKVIIRSILREN 1457

**FIG. 3E**